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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/960,708	09/19/2001	Gerald R. Crabtree	STAN201	4284

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EXAMINER	
MCGARRY, SEAN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/960,708	CRABTREE ET AL.	
	Examiner	Art Unit	
	Sean R. McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-11,15-18,35-44,46 and 47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11, 15-18, 35-44, 46, and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-11, 15-18, 35, 37, 39, 40, and 44 remain rejected under 35 U.S.C. 102(b) as being anticipated by Jiang et al [Carcinogenesis Vol. 14(1):67-71, 1993].

Jiang et al disclose the inhibition of tumor formation in a mouse comprising the administration of FK506 and also disclose that it was known in the art that administration of cyclosprorin A, which is "remarkably similar" in biological properties with FK506, to mice inhibited skin tumor formation in mice (see Figure 1, for example). The prior art methods include all the steps of the instant methods and the effects [inhibiting angiogenesis/vascular development] are considered to be inherent in the prior art methods.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36-44, 46 and 47 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Jiang et al as applied to claims 8-11, 15-18, 35, 37-40 and 45-47 above, and further in view of Flanagan et al.

The instant claims recite the use of cyclosporine, rapamycin and synthetic mimetics and derivatives thereof in the claimed methods.

Jiang et al disclose the inhibition of tumor formation in a mouse comprising the administration of FK506 and also disclose that it was known in the art that administration of cyclosprorin A, which is "remarkably similar" in biological properties with FK506, to mice inhibited skin tumor formation in mice (see Figure 1, for example). The prior art methods include all the steps of the instant methods and the effects [inhibiting angiogenesis/vascular development] are considered to be inherent in the prior art methods. It is clear from the teachings of Jiang et al that it would be obvious to use compounds with common biological properties with FK506 in their methods since it was the common properties of FK506 to cyclosprorin A that caused them to determine the effects of FK506, for example (see page 67, for example).

It is further taught in Flanagan et al that FK506 and cyclosprorin and FK506 have similar properties as is evidenced by their interchangeable use in the methods taught therein, for example. It is further taught that rapamycin is a structural analogue of FK506 and have taught its use a control in experiments utilizing FK506, for example.

The prior art therefore clearly teaches the interchangeable use of Cyclosporin A and FK506 and rapamycin based on their biological properties which would clearly

indicate to one in the art to use compounds with the specific biological properties of cyclosprorin A and FK506 in the method of Jiang et al and furthermore it is clear that one would utilize rapamycin as a control in the methods of Jiang et al, for example, as taught by Flanagan et al.

The invention, as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Applicant's arguments filed 2/23/05 have been fully considered but they are not persuasive. Applicant argues that the amendments to the claims which indicate that the subject has a condition associated with unwanted angiogenesis or having a neoplastic condition overcomes the rejection of record. Applicant argues that the prior art has only disclosed the addition topical administration of FK506 15 minutes prior to the addition of TPA indicates that the "subjects" would not have such a condition. It is noted however, that, for example, Figure 1, clearly shows that mice with tumors were in fact also treated. The mice were treated twice daily for 22 weeks with both TPA and FK506 and it is clear that those treated with TPA and FK506 had less tumors than those treated with TPA alone, for example. See days 15-22, for example. It is clear that mice with tumors were also treated with FK506. Applicant argues that the claims are limited to treating an established condition. The mice have papillomas and FK506 has been administered to those mice that have papillomas. Mice with papillomas have a condition associated with unwanted angiogenesis and have a neoplastic condition. Regardless of whether Jiang

et al specifically appreciated the mechanism of action of the FK506, its action was inherently acting in the mice with existing papillomas. Applicant argues that "it is entirely possible and in no way inconsistent with the asserted teachings of Jiang et al that FK506 has no effect on the growth of TPA-induced papillomas." Applicants' opinion is appreciated but carries no evidentiary weight. This is especially true since the instant specification indicates that FK506 and rapamycin as well as synthetic mimetics thereof inhibit calcinuerin dephosphorylation of NF-ATc (which is applicants asserted mechanism of action(see page 6)). If applicant has evidence that this is not true or that the FK506 administered to the mice of Jiang does not so function, such evidence would be considered. It is assumed that the compounds used in the methods applicants invention function as described in the instant specification whether one appreciates its action or not.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sean R McGarry
Primary Examiner
Art Unit 1635